

Risk factors for impaired healing of the perineal wound after abdominoperineal resection of rectum for carcinoma

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Abstract

Objective Nonhealing perineal wound is an unpleasant complication of surgical excision of the rectum and anus. The aim of the study was to evaluate the risk factors for impaired perineal wound healing after abdominoperineal resection (APR) of rectum for adenocarcinoma, particularly with the increasing use of neo-adjuvant chemoradiation.

Method The study included 38 consecutive patients (29 men, nine women; median age 66 years, range: 43–86), who underwent surgical excision of rectum and anus for adenocarcinoma from 1999 to 2004. Thirty-seven patients underwent APR of rectum and one patient, who developed carcinoma in the background of chronic ulcerative colitis, had panproctocolectomy. Associations between the failure of the perineal wound to heal and a number of patient, tumour and treatment-related variables were evaluated by Pearson chi-square test or Fisher's exact test, as appropriate. A *P*-value of <0.05 was considered significant. Multivariate statistical technique of principal component analysis was also used to identify risk factors and their relative contribution to impaired healing.

Results Impaired healing of the perineal wound was observed in 10 (26%) of 38 patients. In four of them

(11%) the wound remained nonhealed in 1 year after surgery. Preoperative radiotherapy, delayed primary closure of the wound and alcohol consumption in excess of 28 units/week was statistically significantly associated with impaired wound healing. Principal component analysis identified the following seven factors that cumulatively contributed to 96% of impaired healing: (i) distant metastases, (ii) preoperative radiotherapy, (iii) T-stage of the tumour, (iv) smoking, (v) perioperative blood transfusion, (vi) preoperative chemotherapy and (vii) development of side effects of preoperative chemoradiation.

Conclusion Patients who undergo APR of rectum are prone to impaired healing of the perineal wound if radiotherapy is used to treat malignancy prior to surgery and wound closure is delayed. In addition, the wound may not heal in patients with distant metastases, excessive alcohol consumption, present and past smokers and those who suffer adverse effects of preoperative chemoradiation and require blood transfusion.

Keywords Perineal wound healing, abdominoperineal resection, cancer

Introduction

Despite the established role of preoperative downstaging radiotherapy in the management of rectal adenocarcinoma and the resulting tendency to sphincter-preserving surgery [1] abdominoperineal resection (APR) remains a standard procedure for tumours affecting the lower rectum. Unfortunately, such surgery can lead to unpleasant and sometimes long-lasting perineal wound compli-

cations including infection, breakdown, delayed healing and formation of a chronic sinus. Reported perineal morbidity following APR for neoplasia varies from 10% to 40% [2,3]. There are numerous factors believed to be contributing to poor wound healing and neo-adjuvant chemoradiation is among them [4]. The aim of the study was to identify the risk factors for impaired healing of the perineal wound after surgical excision of the rectum and anus for adenocarcinoma.

Method

The study included 38 consecutive patients (29 men and nine women; median age 66 years; range: 43–86) who underwent surgical excision of the rectum and anus for

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adenocarcinoma in our institution between 1999 and 2004. Thirty-seven patients underwent APR and one patient, who developed carcinoma of the upper rectum in the background of chronic ulcerative colitis, had panproctocolectomy. In the patient, who had panproctocolectomy, the tumour was in the upper rectum and in all other cases the tumour was localized in the lower third of the rectum and/or anus (0–5 cm from the anal verge on rigid proctosigmoidoscopy). Preoperative local staging was accomplished by computerized tomography (CT) and/or magnetic resonance imaging (MRI) and distant metastases were excluded by chest X-ray and thoracic and abdominal CT scan. TNM Classification of malignant tumours was used and a surgical technique of total mesorectal excision was employed in all patients. Although surgery was carried out with curative intent, in two patients (5%) hepatic metastases were detected at laparotomy. Of 38 patients, 15 (39%) with tumours confined to the rectum were treated by radical surgical resection alone. Four patients (11%) with clinically mobile and resectable tumours received a short course of preoperative radiotherapy as part of a trial given as an external beam radiation in a total dose of 25 Gy over 1 week and followed by radical surgical resection. The remaining 19 (50%) of 38 patients had clinical and/or radiological features of tumour fixation or extramural invasion and received a long-course radiotherapy, which was given as an external beam radiation of 45–50 Gy over a period of 5 weeks. Two patients received a further boost of brachyradiotherapy and one of them required Iridium implant increasing the total dose of radiation to 100 Gy. In 14 (37%) patients this long-course downstaging radiotherapy was combined with chemotherapy: 5-fluorouracil administered during the first and last week of radiation treatment. In addition, one patient was given weekly Irinotecan as a part of a trial. Subsequent APR was carried out in 6–8 weeks on completion of radiotherapy. Perineal wound was managed by primary closure in 29 (76%) patients and delayed primary closure in nine (24%) patients with the aim to achieve its healing by primary intention. Suction drainage of the wound was used in all cases. Impaired healing of the perineal wound, the end-point of the study, was defined as clinically evident dehiscence and/or persistent infection. Failure of the wound to heal by 6 weeks postoperatively was evaluated with respect to a number of patient, tumour and treatment variables. Patient-related factors included age, gender and pre-existing conditions, such as diabetes mellitus, ischaemic heart disease (IHD), chronic obstructive pulmonary disease (COPD), systemic corticosteroidal therapy, past and present tobacco smoking and weekly alcohol consumption. Clinicopathological tumour characteristics included in the analysis were its distance

from the anal verge, TNM stage and the completeness of excision. Treatment-related variables included preoperative radiotherapy and chemotherapy, complications of neo-adjuvant chemoradiation, adverse intra-operative events, unplanned additional surgical procedures, perioperative blood transfusion, development of early postoperative complications and management of the perineal wound by primary or delayed primary closure.

Statistical analysis

Associations between impaired perineal wound healing and the above variables were evaluated by Pearson chi-square test or Fisher's exact test, as appropriate. A P -value of <0.05 was considered significant. Multivariate statistical technique of principal component analysis (rotation method: Varimax with Kaiser normalization) was also used to identify risk factors and their relative contribution to impaired healing. More detailed description of the principal component analysis can be obtained elsewhere [5]. Statistical analysis was carried out using SPSS, version 14.0, computer software (SPSS, Chicago, IL, USA).

Results

Twenty-eight (74%) of 38 patients had uncomplicated healing of the perineal wound. In 10 (26%) patients the perineal wound failed to heal resulting in its dehiscence, chronic sepsis and/or persistent sinus. In four of them (11%) the wound remained nonhealed 1 year after surgery. One patient died of cardio-respiratory complications 1 month after surgery, constituting surgical mortality of 3%.

Univariate analysis showed no adverse influence of patient's age on wound healing. Weekly alcohol consumption in excess of 28 units had statistically significant association with impaired healing ($P = 0.048$) but all other patient-related variables had no negative effect (Table 1). None of tumour-related factors influenced wound healing (Table 2). Analysis of treatment-related variables showed that preoperative radiotherapy and delayed primary closure of the wound were associated with poor perineal wound healing (Table 3). Five (13%) patients suffered side effects of neo-adjuvant chemoradiation, including radiation proctitis, perianal dermatitis, cystitis, enteritis and pyrexia of unknown origin. Ten patients (26%) suffered adverse intra-operative events, defined by operating surgeon as pelvic haemorrhage (two patients), rectal perforation and pelvic faecal contamination (four patients), faecal soiling of the perineal wound (two patients) and technical difficulties because of local tumour invasion (two patients). None of these influenced

Table 1 Healing of the perineal wound in relation to patients' characteristics.

	Number of patients	Nonhealed perineal wound (%)	P-value
Gender			
Male	29	27.6	0.560
Female	9	22.2	
Diabetes mellitus			
No	37	27.0	0.737
Yes	1	0.0	
COPD			
No	30	30.0	0.306
Yes	8	12.5	
IHD			
No	33	27.3	0.604
Yes	5	20.0	
Corticosteroids			
No	37	27.0	0.737
Yes	1	0.0	
Smoking			
No	20	25.0	0.737
Yes	18	27.8	
Alcohol (>28 units)			
No	34	20.6	0.048
Yes	4	75.0	

Table 2 Healing of the perineal wound in relation to tumour characteristics.

	Number of patients	Nonhealed perineal wound (%)	P-value
Distance from anal verge (cm)			
0-1	8	37.5	0.898
1≤2	10	30.0	
2≤3	10	30.0	
3≤4	6	16.7	
4≤5	3	0.0	
14	1	0.0	
T-stage			
T1	6	33.3	0.767
T2	8	25.0	
T3	22	22.7	
T4	2	50.0	
N-stage			
N0	27	22.2	0.305
N1	11	36.7	
N2	0		
M-stage			
M0	36	25.0	0.426
M1	2	50.0	
Completeness of excision (histologically)			
Clear resection margins	32	21.9	0.174
Positive resection margins	6	50.0	

Table 3 Healing of the perineal wound in relation to treatment characteristics.

	Number of patients	Nonhealed perineal wound (%)	P-value
Radiotherapy			
No	15	6.7	0.028
Yes	23	39.1	
Chemotherapy			
No	24	20.8	0.084
Yes	14	42.9	
Complications of chemoradiation			
No	33	24.2	0.396
Yes	5	40.0	
Adverse intra-operative event			
No	28	25.0	0.530
Yes	10	30.0	
Additional procedure			
No	35	25.7	0.612
Yes	3	33.3	
Blood transfusion			
No	23	26.1	0.627
Yes	15	26.7	
Postoperative complications			
No	20	20.8	0.315
Yes	14	35.7	
Wound closure			
Primary	29	13.7	0.005
Delayed primary	9	66.7	

perineal wound healing. Additional unplanned procedures proved necessary in three (8%) patients. These consisted of ureteric stenting and liver biopsy and had no negative effect on wound healing. Major postoperative complications were encountered in seven (18%) patients and included haemorrhage (three patients), acute gastric haemorrhage from stress ulcers (one patient), colostomy necrosis (one patient), urethral fistula (one patient), bronchopneumonia (one patient) and deep venous thrombosis (one patient). There were seven (18%) minor postoperative adverse events, such as acute urinary retention, urinary tract infection, respiratory infection and short-lasting cardiac arrhythmia. Development of early postoperative complications did not have statistically significant association with impaired wound healing.

Principal component analysis identified the following seven factors that cumulatively contributed to almost 96% of impaired healing: (i) distant metastases, (ii) preoperative radiotherapy, (iii) T-stage of the tumour, (iv) smoking, (v) perioperative blood transfusion, (vi) preoperative chemotherapy and (vii) development of side effects of preoperative chemoradiation. Their relative contribution to impaired healing is shown in Table 4.

Table 4 Relative contribution of variables to impaired healing of the perineal wound on the basis of the principle component analysis.

Factor	Contribution to impaired healing (% of variance)	Cumulative contribution to impaired healing (%)
1. Distant metastases (M-stage)	19.6	18.5
2. Preoperative radiotherapy	17.0	36.6
3. T-stage of tumour	14.8	51.4
4. Smoking	13.8	65.2
5. Blood transfusion	11.0	76.2
6. Preoperative chemotherapy	9.8	86.0
7. Complications of chemoradiation	9.6	95.6

Discussion

There are many local and systemic factors, which may interfere with the process of healing, including that of the perineal wound. In our study adverse influence of preoperative radiotherapy was confirmed by both chi-square statistics and principal component analysis. This finding is of importance because, following compelling evidence of reduction in local recurrence [6–9] and improvement in survival [8,10,11], preoperative radiation has become widely used not only in downstaging irresectable adenocarcinomas prior to surgery, but also in the treatment of potentially resectable locally advanced tumours. Although debate continues on its benefit in resectable and mobile rectal tumours, recommendations have been passed to consider preoperative irradiation in all but T1 adenocarcinomas, particularly in patients, who are likely to require APR [12]. Radiation-associated perineal complications were observed in several randomized-controlled trials using short- [2,13] and long-course [14] radiotherapy regimens. Thus, Swedish Rectal Cancer Trial showed twofold increase of the rate of perineal wound infection from 10% to 20% [2]. Dutch Colorectal Cancer Group observed perineal complications in 31% patients in whom perineum was exposed to short-course radiation but still considered shielding of the perineum undesirable in patients planned for APR out of fear of local recurrence [13]. Polish Colorectal Study Group showed even slightly higher rates of delayed perineal healing and infection after short-course radiotherapy (29%) in comparison with long-course chemoradiation (21%), although the difference did not reach statistical significance [15]. Christian *et al.* [16] observed major and minor perineal wound complications in 47 (35%) of 136 patients operated for rectal and anal malignancy. In our series, the incidence of delayed wound healing in radiated patients was 39%, compatible with the previous reports.

Surgeons differ widely in their handling of the perineal wound after APR. Miles who described the operation in

1908 [17] initially practised wound closure around large drains but abandoned this method in favour of open wound due to high morbidity. There is still no universal consensus of opinion about the optimal method of perineal wound management with regard to its closure, drainage and irrigation. Thus, Mazeir *et al.* [18] found no difference in outcome between the primary closure and open packing of the wound in a series of 288 patients and others advocated primary closure and drainage [3,19,20]. Although the wound may have to be packed to control troublesome haemorrhage and in cases of faecal contamination [21] delayed primary closure scored unfavourably in our experience. Although confounding, as in any other study, is impossible to eliminate completely, the choice of the delayed wound closure in our series was largely a matter of personal preference of operating surgeon rather than a direct consequence of bleeding or faecal soiling. Authors of this study also accept that some of the risk factors might have been linked, for example, neo-adjuvant radiation was mainly used because of the advanced T-staging and principal component analysis incriminated both variables in delayed healing. Age [4] and other factors affecting host resistance, such as diabetes mellitus [16], systemic steroids [4] have been traditionally blamed for poor healing. None of them mattered in our series apart from excessive alcohol consumption. Radice *et al.* [22] previously commented on difficulties in estimation of relative contribution of radiation to the risk of complications. We have attempted to overcome this problem using principal component analysis as a statistical tool not only to identify risk factors, but also to calculate their separate percentage contribution to poor wound healing. For example, the influence of preoperative radiation was higher (17.0%) than blood transfusion (11.0%). This methodology identified that just seven out of examined variables were cumulatively responsible for almost all (96%) nonhealed perineal wounds. When several of the above factors are encountered, predicting poor wound healing, an immediate plastic reconstruction of the radiated perineum could be the answer to prevent

long-lasting wound-related complications. Reports on primary myocutaneous flap closure to promote healing of radiated perineum have been encouraging [22,23].

Conclusions

Patients who undergo APR are prone to impaired healing of the perineal wound if radiotherapy is used to treat malignancy prior to surgery and wound closure is delayed. In addition, the wound may not heal in patients with distant metastases, excessive alcohol consumption, present and past smokers and those who suffer adverse effects of preoperative chemoradiation and require blood transfusion.

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